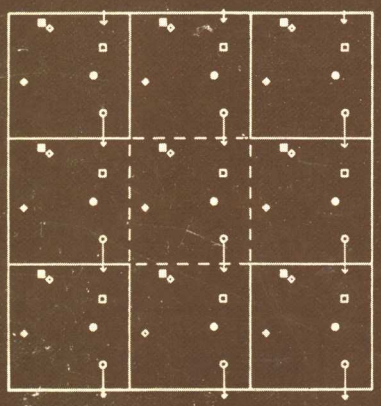
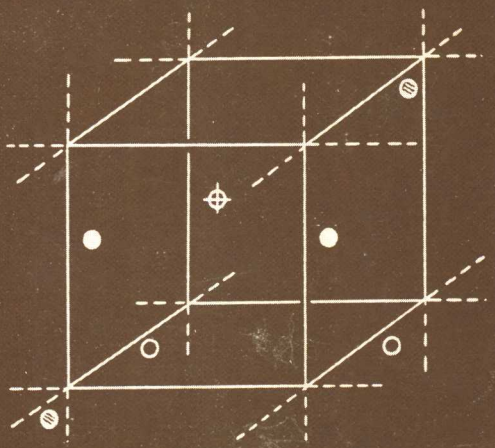
Chemistry by Computer

An Overview of the Applications of Computers in Chemistry





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Preface

Computers have been applied to problems in chemistry and the chemical sciences since the dawn of the computer age; however, it is only in the past ten or fifteen years that we have seen the emergence of computational chemistry as a field of research in its own right. Its practitioners, computational chemists, are neither chemists who dabble in computing nor programmers who have an interest in chemistry, but computational scientists whose aim is to solve a wide range of chemical problems using modern computing machines.

This book gives a broad overview of the methods and techniques employed by the computational chemist and of the wide range of problems to which he is applying them. It is divided into three parts. The first part records the basics of chemistry and of computational science that are essential to an understanding of the methods of computational chemistry. These methods are described in the second part of the book. In the third part, a survey is given of some areas in which the techniques of computational chemistry are being applied. As a result of the limited space available in a single volume, the areas covered are necessarily selective. Nevertheless, a sufficiently wide range of applications are described to provide the reader with a balanced overview of the many problems being attacked by computational studies in chemistry.

It is intended that this book should prove useful to a wide variety of scientists. Undergraduate chemists will use it as an introduction to computational chemistry. Experimental research chemists should use this book to gain an understanding of the ways in which the techniques of computational chemistry can aid their research programs. These techniques have potential applications in fields as diverse as radioastronomy and astrochemistry, solid-state and nuclear physics, organic synthetic chemistry, catalysis, molecular biology, pharmacology, and molecular electronics. Although the present volume does not provide a detailed survey of any of these fields, it does present a broad overview of many of them. A bibliography is given at the end of each chapter to enable the interested reader to investigate a particular method or application in more detail.

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PART I

BASICS

Chapter 1

Introduction

> I would like to emphasize strongly my belief that the era of computing chemists, when hundreds if not thousands of chemists will go to the computing machine instead of the laboratory, for increasingly many facets of chemical information, is already at hand.
> — ROBERT S. MULLIKEN

The traditional view of a chemist is one of a white-coated, rather untidy individual working in a cluttered laboratory with a distinctly unhealthy atmosphere. It is an image with a long history dating from the heyday of the Industrial Revolution. These "traditional" chemists played a key role in the industrialization, which, as we all know, changed first the face of Britain and then the rest of the world over the last two hundred years.

The nineteenth-century chemists laid down the chemical basis of much of modern industry — the steel industry, the petrochemical industry, fertilizers, plastics, etc., and they developed many colorful dyes, which were used to brighten the products of the cotton mills of Lancashire and the wool factories of Yorkshire. At the same time, the firm foundations upon which modern chemical theories are based were being built and chemistry was gradually evolving into the exact science it is today.

In the second half of the twentieth century, society is

experiencing a new revolution on a similar scale. As was the case with the Industrial Revolution, the "Computer Revolution" is having an overwhelming and comprehensive impact on our society, affecting individuals in all walks of life. And, like his predecessor, the contemporary chemist is playing a full and impressively versatile role in this new period of innovation and change.

This book provides an overview of some of the many applications which computers have found and, indeed, are still finding in chemistry and the chemical sciences. It is intended to give a selective coverage of a diverse but nevertheless representative range of topics from *ab initio* quantum-mechanical calculations of the electronic structure of small molecules, to the determination of the bulk properties of chemical systems by means of Monte Carlo simulation techniques, and to the computer-aided design of synthetic routes in organic chemistry. Areas not covered are those which are not specific to chemistry, such as the use of computers, and in particular microcomputers, in the real-time control of experiments, the routine analysis of data derived from experiment, the use of computers in teaching, and the use of computers in searching the literature.

Chemistry is, and has in fact long been, one of the primary areas of application for computers in scientific research. Developments in computational quantum chemistry, in particular, have frequently gone hand-in-hand with developments in computer technology and in computer science. Other fields of computational chemistry have been maturing in recent years as chemists continue to identify the advantages that may result from the application of computers and computational techniques to improve their research capabilities. Computational chemistry can often afford information which is not available from experiment. It can sometimes provide a deeper understanding of chemical problems. Further, it can frequently be more economic to adopt a computational rather than an experimental approach to a particular problem. However, computational and experimental studies often afford complementary information about a chemical system.

The book is divided into three parts. Chapters 1–3 discuss the basic principles of chemistry and of computing that are fundamental to the applications of computers in chemistry. Chapters 4–7, which constitute the second part of the book, describe some of the methods employed by the computational chemist. Chapter 4 is concerned with computational quantum chemistry, in which the properties of atoms and molecules are determined by solving the basic equations of quantum mechanics that govern the behavior of the component electrons and nuclei. For larger molecules the techniques of computational quantum chemistry become intractable and the computational realization of the familiar ball-and-stick models of molecules are employed to investigate their structure and properties. This is the method of molecular mechanics and it is discussed in Chapter 5. In Chapter 6, the use of computers in the study of chemical reactions is discussed, starting with the description of chemical reactions at a molecular level, then considering the solution of chemical kinetics equations, and finally the computer-aided design of synthetic routes in organic chemistry. In Chapter 7, the computational study of the bulk properties of matter are considered. Monte Carlo and molecular-dynamics simulation techniques are described. In the final part of the book some of the areas in which the techniques of computational chemistry described in Part II are being employed are overviewed. It is, of course, impossible in a single volume to mention all areas of computational chemistry. In Chapter 8, the study of interstellar molecules and of interstellar reaction processes is described. The rapidly developing field of computational pharmacology is discussed in Chapter 9. Chapter 10 addresses some of the applications of the techniques of computational chemistry in the field of molecular biology. The final chapter is devoted to some of the possible directions in which computational chemistry may proceed in the future. As the Nobel Prize winning chemist, Robert S. Mulliken, foresaw, the computer is going to be an increasingly valuable source of chemical information to the chemist and a particularly powerful agent of change in the future of chemistry as a whole.

Chapter 2

Chemistry by Computer

2.1. Computational Chemistry

Today, the situation has been reached where, in many cases, the computational chemist can substitute the computing machine for the test tube. Not that the computational approach to the study of chemistry should be regarded as a rival to the traditional experimental techniques. Often the two approaches are complementary, one approach providing data which are not available from the other, and vice versa. Sometimes an experiment may be considered too dangerous, or indeed impossible, to perform in the laboratory and the methods of computational chemistry then provide the only route to the required chemical information. For example, beryllium compounds are notoriously difficult to work with in the laboratory, not least because of their toxicity, while the beryllium atom is rather easily handled by the methods of computational quantum chemistry since it contains only four electrons. Many compounds are too reactive to be isolated and cannot be studied by standard laboratory techniques, such as infrared spectroscopy or nuclear magnetic resonance. Computational studies of unstable species can usually be performed with no more difficulty than the study of similar stable species.

When computational studies of a series of atoms, molecules, or ensembles of atoms or molecules are performed, information can often be obtained that is of help in rationalizing the observed properties. Useful chemical concepts emerge and can be used to rationalize vast quantities of data. Such concepts can be of great value in the planning of future studies of similar atoms and molecules.

Laboratory experiments can be both expensive and time-consuming. The use of the methods of computational chemistry rather than an experimental approach to the determination of chemical properties can increasingly be justified on economic grounds. In discussing the application of the methods of computational quantum chemistry to biological molecular systems M. W. Brown, writing in *The New York Times* (September 18, 1979), pointed out that, "Because of the shortcuts the method offers in custom-designing chemicals with important new properties, the method has attracted the attention of doctors and drug manufacturers, industrial chemists, national and private health agencies, and the Department of Defense, among other groups."

The description of a given chemical system by computational techniques requires the formulation of a physical model. The complexity of this model will be constrained by the complexity of the chemical system being considered. If we are interested in the properties of a single molecule, such as a radical in interstellar space or an ion which is believed to catalyze certain reactions in the upper atmosphere, then we can treat the entire system quantum mechanically from first principles. We can perform an *ab initio* calculation to determine the structure and properties of a small molecule from the basic laws of quantum mechanics. If, on the other hand, we are interested in bulk properties, such as defects in a crystal or the thermodynamic properties of liquid argon, then having no possibility of studying the motion of a mole of argon atoms in a computer simulation (1 mole contains 10^{23} atoms) even within the framework of classical mechanics, we have to resort to statistical methods. To perform such a study, we need to have a detailed knowledge of the interactions between a single pair of

atoms or molecules; this can often be obtained from *ab initio* calculations. Clementi and his co-workers, writing in the *International Journal of Quantum Chemistry* (Vol. 16, p. 409), summarized the situation as follows: "Theoretical chemistry should attempt to provide an overlapping set of models to describe a chemical system of any degree of complexity. Computational chemistry, a much younger subject, attempts both to provide operational techniques for solving such models and to test for the validity of the models by comparing simulated and experimental data."

Ultimately, all applications of computational chemistry rest on our knowledge of fundamental laws of nature. It is the purpose of this chapter to provide a very brief overview of the basic physics and chemistry which is necessary to an understanding of the techniques of computational chemistry. Obviously, it is impossible in the space available to provide an in-depth discussion; indeed such a discussion would take us too far from the main purpose of this book. The interested reader will find further information in the excellent texts included in the bibliography at the end of this chapter.

2.2. Isolated Atoms and Molecules

Typically, an atom has a size of the order of 10^{-10} m. It consists of a single heavy nucleus with positive charge Z, where Z is the atomic number, surrounded, in its neutral state, by Z electrons each with a single negative charge. The nucleus provides most of the mass of the atom, the electron being some 2000 times lighter than the protons and neutrons that comprise the nucleus. The electrons, however, give the atom most of its bulk and determine most of its chemical properties. The systematic variation of the properties of atoms with atomic number is usually emphasized by arranging them in the well-known periodic table as shown in Figure 2.1.

Molecules consist of groups of atoms joined together by chemical forces. They can range in complexity and size from a simple diatomic molecule, such as the hydrogen molecule (H_2)